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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/259,389	02/26/99	GEORGOPOULOS	K 10287/043001
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LOUIS MYERS
FISH & RICHARDSON PC
225 FRANKLIN STREET
BOSTON, MA 02110-2804

NM12/0329

EXAMINER

WOITACH, J

ART UNIT

PAPER NUMBER

1632

DATE MAILED:

03/29/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action SummaryApplication No.
09/259,389Applicant(s)
Georgopoulos et al.Examiner
Joseph WeitachGroup Art Unit
1632☐ Responsive to communication(s) filed on _____.☐ This action is **FINAL**.☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims☒ Claim(s) 1-17 is/are pending in the application.Of the above, claim(s) 6-9, 12, 14, and 17 is/are withdrawn from consideration.☐ Claim(s) _____ is/are allowed.☒ Claim(s) 1-5, 10, 11, 13, 15, and 16 is/are rejected.☐ Claim(s) _____ is/are objected to.☐ Claims _____ are subject to restriction or election requirement.**Application Papers**☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.☐ The drawing(s) filed on _____ is/are objected to by the Examiner.☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.☐ The specification is objected to by the Examiner.☐ The oath or declaration is objected to by the Examiner.**Priority under 35 U.S.C. § 119**☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been☐ received.☐ received in Application No. (Series Code/Serial Number) _____.☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).**Attachment(s)**☒ Notice of References Cited, PTO-892☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____☐ Interview Summary, PTO-413☒ Notice of Draftsperson's Patent Drawing Review, PTO-948☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

Applicants amendment filed February 17, 2000, Paper No. 5, has been entered.

Acknowledgment is made of Applicants response to Restriction Requirement. Group I has been elected without traverse. Claims 1-5,10, 11, 13, 15, 16 are pending and are under current examination.

Claim Objections

Claim 11 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15 and 16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

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The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). See MPEP 2164.01(a).

With respect to claims 15 and 16, the application is silent with respect to the role of Helios in any disorder or any examples that point to any specific function of Helios. Sequence homology demonstrates that Helios is a member of the T cell-restricted Ikaros family and experiments show that Helios can interact with the other family members. It has been demonstrated that the absence of one of the family members, Ikaros, can lead to development disorders. However, this is complicated by the fact that expression of some mutant forms of Ikaros produce effects different than that of the complete absence, suggesting complicated mechanisms of action or control of Ikaros. Hahm *et al.* point out that gene disruptions of Ikaros have shown 'that Ikaros isoforms carry out critical functions during the development of B and T lymphocytes...[n]evertheless,...the precise intracellular functions of Ikaros almost certainly will be difficult to elucidate' (page 792; Discussion). Similar experiments have not been done for Helios and so no examples for a function of Helios exist. Further, the expression pattern in different tissues and co-localization of the protein is different from that of Ikaros suggesting a different role for the Helios gene product. Further, Hahm *et al.* point out that even though work to elucidate the role of Ikaros has been done, 'the specific functions of Helios and of the Helios-Ikaros complex remain unknown' and 'remain to be elucidated' (page 792; discussion). While deletion or mutations of Helios may

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produce similar effects seen for that of Ikaros, empirical experiments must be done to demonstrate this fact.

Since Helios is a member of a larger family of genes, one may suggest a role or function based on family member similarity, however, the expression pattern of the family members differ. Kelly *et al.* state that '[w]hereas Ikaros and Aiolos are predominantly expressed in hematopoietic sites, Helios is also expressed elsewhere' (page 514; last paragraph). Different tissue distribution and co-localization of the proteins suggests a different role for the Helios gene product than that of the other family members. While the role of Helios may be important in hematopoietic development, without the detailed experiments performed like those of other Ikaros family members, one can not predict the role or function of Helios. Finally, Kelly *et al.* state '[m]utational analysis of the Helios gene will help to dissect its role in regulating progenitor development in the hematopoietic system' (page 514; final paragraph), suggesting the function of Helios is not known, and that one can not relate changes in Helios expression or mutations of the gene to any sort of risk towards any disorder.

Further, with respect to claim 15, even if the function of Helios was known, or what disease is associated with a particular expression or form of Helios, the *in vivo* or *ex vivo* gene therapy methods to deliver the DNA or corresponding peptide would involve undue experimentation. At the time the invention was made, methods detailing the successful implementation for the administration of DNA were not routinely obtainable by those skilled in the art. This is reflected by two subsequently published reviews. Verma *et al.* teach that as of

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1997, "there is still no single outcome that we can point to as a success story" (page 239, col. 1). The authors go on to state, "Thus far, the problem has been an inability to deliver genes efficiently and to obtain sustained expression" (page 239, col. 3). Anderson (1998) states that "there is still no conclusive evidence that a gene-therapy protocol has been successful in the treatment of a human disease" (page 25, col 1) and concludes, "Several major deficiencies still exist including poor delivery system, both viral and no-viral, and poor gene expression after genes are delivered" (page 30).

In view of the of the lack of guidance, working examples, breadth of the claims, skill in the art and state of the art at the time of the claimed invention, it would require undue experimentation by one of skill to practice the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-5, 10, 11, 13, 15 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claims 3-5 are vague and unclear in the recitation of "Helios polypeptide" because SEQ ID NO: 1, 3 and 5 code for unique helios polypeptides which contain different amino acid sequences. It is not clear to which specific sequence is being referred to or if the product claimed

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must satisfy conditions for all three sequences. In each case the differences could result in a different nucleic acid for hybridization (claim 3), different antibody to a unique sequence (claim 4) or different peptide (claim 5). Without a functional property to define Helios, it is not clear what makes polypeptide a 'Helios polypeptide'.

Claim 3 is vague and indefinite in the recitation of "under high stringency conditions" because the conditions are not described and so the metes and bounds are not defined.

Claims 15 and 16 are vague and indefinite because it is not clear what disorder is being treated or diagnosed. Neither the claim nor the specification describe Helios related disorders.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

a person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-5 are rejected under 35 U.S.C. 102(a) as being anticipated by Hahm *et al.*

Claims 1-5 are drawn to a polynucleotide which is at least 60% homologous to SEQ ID NO: 1, 3 or 5 which encode a Helios polypeptide. Hahm *et al.* teach the mus musculus helios mRNA which shares >60% homology with the three SEQ ID.

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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) a patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 10, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hahm *et al.* in view of Molnar *et al.*

Hahm *et al.* teach a helios sequence which can encode a helios polypeptide, however, they do not teach to put this sequence into a vector and express the protein in a cell. Molnar *et al.* teach a related protein to helios, in which the coding polynucleotide is inserted into a vector and is expressed in a cell. The polypeptide produced in the cell is detected by antibodies made to the specific peptide. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the sequence of Hahm *et al.* with the methods presented in Molnar *et al.* to clone the coding region of helios into a vector, then transfect the vector into a cell to express the protein. One having ordinary skill in the art would have been

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motivated to combine these two replacement materials to provide for a means to produce the protein and study its function the *in vitro* conditions of the cell. There would have been a reasonable expectation of success given the results of Molnar *et al.* to clone the coding region of helios of Hahm *et al.* into a vector to express the protein in a cell.

Thus, the claimed invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jasmine C. Chambers, can be reached at (703)308-2035.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-0196.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Woitach



BRUCE R. CAMPELL
PRIMARY EXAMINER
GROUP 1800